

REMARKS/ARGUMENTS

Applicants believe no new matter is added by these amendments to the specification and claims. Claims 1-70 have been canceled. New claims 71-78 have been added. After entry of the present amendments, Claims 71-78 will remain in this application.

Amendments to the claims.

Support for 60%, 80% and 95% identity to the presently claimed polypeptides is provided on, for example, page 55, lines 20-23.

Support for a “transgenic plant [that] is more likely to have survived seven to eight days of a drought treatment, rewatering, and two to three days of a recovery period than the control plant” is provided, for example, on page 147, line 7 through page 148, line 1, and the following table, Table 10 on page 148, the third row (“G922...[survival rating] 1.406”).

Response to specific items within the Office action.

Item 5. Rejection under 35 USC 112, first paragraph, written description.

Applicant believes the amendment of the present claims in part avoids this rejection, and the rejection is also traversed for the reasons detailed below..

Applicants identified closely related sequences with at least 60% identity to SEQ ID NO: 4. These sequences include soybean sequences G3810, SEQ ID NO: 212, and G3811, SEQ ID NO: 214. The latter two sequences are described as “G922 equivalents” (page 119, lines 13-15), and equivalents are defined using the TIGR definition, restated on page 17, lines 16-20.

The percentage identities of these sequences to the G922 sequence are at least about 60%, as determined by an analysis conducted with Accelrys Gene v. 2.5 (2006) with the following parameters:

Pairwise Matrix: GONNET
Align Speed: Slow
Open Gap Penalty: 10.000
Extended Gap Penalty: .100
Multiple Matrix: GONNET
Multiple Open Gap Penalty: 10.000
Multiple Extended Gap Penalty: .05
Delay Divergent: 30
Gap Separation Distance: 8
End Gap Separation: false
Residue Specific Penalties: false
Hydrophilic Penalties: false

Hydrophilic Residues: GPSNDQEKR
Alignment Score 5670

Using these parameters, the Accelrys program indicated the following percentage identities:

	<u>G922</u>
G922:	100.0
G3810:	65.9
G3811:	62.8

The specification describes the genus of sequences that are homologous to the listed sequences and share at least about 60%, or at least about 80%, or at least about 95% amino acid sequence identity over the entire length of the polypeptide or the homolog. The sequence species G922, G3810 and G3811, having been derived from diverse plant species, were described in the instant application as SEQ ID NOs: 4, 212, and 214. The attached declaration provides evidence that two soybean sequences closely related to SEQ ID NO: 4 also confer the function of improved water deficit tolerance. These are the only orthologs of G922, SEQ ID NO: 4, that have been tested in plants to date.

Applicants thus meet the requirements of the instant rejection (page 4, paragraph 2) by describing variants of instant SEQ ID NO: 4 that have the equivalent function in a transgenic plant.

This rejection also indicates that the “instant claims recite no conserved structure that produces such an equivalent function” (page 4, paragraph 2) . However, three distinct conserved domains are described and associated with each of these species, found in Table 1 beginning on page 34. Percentage identity is a structural relationship, and Applicants have shown how the claimed percentage identities related to conserved function.

In light of these amendments, arguments and experimental observations confirming Applicants’ disclosure and claims, Applicants request that the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, be withdrawn.

Item 6. Rejection under 35 USC 112, first paragraph, enablement

Applicant believes the amendment of the present claims avoids this rejection under 35 U.S.C. §112, first paragraph, and the rejection is also respectfully traversed for the reasons set forth below.

The specification provides a genus of sequences that are homologous to the listed sequences and share at least about 60%, or at least about 80%, or at least about 95% amino acid sequence identity over the entire length of the polypeptide or the homolog. The sequence species G922, G3810 and G3811, having been derived from diverse plant species, were provided in the instant application as SEQ ID NOs: 4, 212, and 214, along with methods for the isolation of related sequences. Three distinct conserved

domains are associated with each of these species, found in Table 1 beginning on page 34. It would be a matter of routine for the skilled artisan to use each or all of these domains to identify structurally and functionally related sequence species, and said artisan would have a reasonable expectation of success in isolating and making use of similar sequences to produce the claimed functions, particularly in light of Applicants' success in doing so.

Accordingly, Applicant respectfully requests that the rejection of the claims under 35 USC 112, first paragraph, for lack of enablement, be withdrawn.

Item 7. Rejection under 35 USC 103 (a)

Applicants respectfully traverse the present rejection.

The Examiner repeats the rejection under 35 USC 103(a) based on the teachings of Pysh (1999) Plant J. 18:111-119. However, the sequence taught by Pysh is not the same sequence as is found in the present claims, lacking these 157 amino acids at the N-terminus, including 24 amino acids that make up part of the first SCR domain (underlined):

MVAMFQEDNGTSSVASSPLQVFSTMSLNRPTLLASSSPFHCLKDLKPEERGLYLIHLLLTCAHNVASGSL
QNANAALQLSHLASPDGDTMQRIAAYFTEALANRILKSWPGLYKALNATQTRTNNVSEEIHVRRLLFFEM
FPILKVS YLLTNRAILE

In response to this failure of the Pysh teaching and Applicants assertion that there is no teaching of transgenic plants or motivation to produce the instantly claimed plants, the Examiner argues that "KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness (original emphasis)", in reference to *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007).

The Examiner also cites *Ex parte Smith* USPQ2d 1740, 82 USPQ2d at 1396 to bolster the assertion that "it would have been obvious to one of ordinary skill in the instant art to isolate the complete coding region and transform a plant, especially using a constitutive or a root-specific promoter".

Applicants note that there is no assertion in either *KSR* or *Ex parte Smith* that the respective opinions extend to biotechnological arts, which have been held (as Applicants have been reminded by this Examiner many times) to be less predictable than mechanical arts. However, in *In re Deuel*, 35 U.S.P.Q.2d 1210 (Fed. Cir. 1995), which does pertain to the biotechnological arts, the Federal Circuit reversed the USPTO and held that claims directed to polynucleotides that encode a particular polypeptide should not be considered obvious in view of a prior art reference that taught methods of cloning, when combined with a reference that taught a *partial* amino acid sequence of the polypeptide. The Federal Circuit stated that because the claims at issue were directed to a specific chemical structure (i.e. a

nucleotide sequence), a *prima facie* case of obviousness should be based on teachings in the prior art that suggest the particular structure being claimed, irrespective of whether the methods used to arrive at the particular chemical structure were obvious. The Federal Circuit noted that, “[n]ormally a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound.” In the absence of such structural similarity in the prior art, the court held that a rejection based on obviousness is not proper. Furthermore, the court in *Deuel* noted that the “...PTO’s focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not methods.... [T]he issue is the obviousness of the claimed compositions, not of the method by which they are made.” Accordingly, the Federal Circuit was clear in *Deuel* that “...the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious...”

As to the concept that it would have been obvious to isolate a complete coding region and transform a plant, Applicants note that gene expression may not be a reliable indicator of gene function, and expression should not be used to infer function without rigorous testing. For example, it is well accepted based on many microarray analyses that hundreds of genes may be up- or down-regulated in response to a stress, but only a small proportion of these, if any, may actually be used to confer stress tolerance. By way of a specific example, constitutive expression of the COR15a gene enhances freezing tolerance at the chloroplast and cellular (protoplast) level, but COR15a expression alone does not result in a detectable increase in freezing survival of whole plants. These findings are not surprising given the results of genetic analyses indicating that freezing tolerance is a multigenic trait involving genes with additive effects (Thomashow (1998) *Plant Physiol.* 118: 1-8).

Furthermore, contrary to the general assertion that KSR applies, the cited *Pysh* reference does not provide a complete sequence or a plant with either established functions or the functions instantly claimed. This conflicts with established practice *and* KSR. The [Supreme] Court quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that “[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” KSR, 550 U.S. 82 USPQ2d at 1396. MPEP 2141(III). Contrary to what has been done in the present rejection, in KSR the Supreme Court repeatedly emphasized its focus on obviousness of combinations of known components: “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results”. (Id. at 1739). Applicants assert that *Pysh* alone, with its incomplete sequence lacking

157 amino acids, including 24 amino acids that make up part of the first SCR domain, cannot be used to predict the instant results. This contrasts with a prerequisite for establishing obviousness with a finite number of identified, predictable solutions.

KSR: “When a patent simply arranges old elements with each performing *the same function it had been known to perform*, and yields no more than one would expect from such an arrangement, the combination is obvious”. Id. (quoting *Sakraida v. AG Pro, Inc.* 425 U.S. 273, 282 (1976), *emphasis added*). Pysh does not teach a “function it had been known to perform”. How can a partial sequence combined with a hypothetical arrangement (i.e., a hypothetical transgenic plant) that never previously existed in nature and with no associated functions taught in this art, yield “more than one would expect from such an arrangement”? How can you expect more from something that never existed? How would you test for surprising results, and, absent perfect hindsight, how would you recognize them?

KSR: “[A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions”. Id., *emphasis added*. Again, Pysh lacks a complete sequence, and even the partial sequence lacks any established functions, let alone the claimed structurally-related functions.

And, significantly, KSR established that: “a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the art”. Id., at 1741. Since there are no known functions of the partial protein taught by Pysh, and since no plant overexpression the G922 sequence was known in the art, the cited elements should not be associated with each one another as the basis of an obviousness rejection.

Thus, the skilled artisan would have been unable to predict function associated with the combination, and the instant improvement is much more than the “predictable use of prior art elements”. Applicants also assert that the present rejection attempts to make a case for obviousness merely by demonstrating that its elements were, independently, known in the art, contrary to the reasoning in *KSR v. Teleflex*. Alternatively, the present Office action asserts that, finding the partial sequence and armed with the knowledge that this partial sequence may be expressed in a plant, it would have been obvious to isolate the complete coding sequence, then transform a plant, and presumably, then test the plant for a useful function.

Accordingly, Applicant respectfully requests that the rejection of the claims under 35 USC 103(a) be withdrawn.

Item 8. Rejection under 35 USC 103 (a)

Applicants respectfully traverse the present rejection.

The same arguments presented above also apply to Benfey et al., cited as the basis of this rejection. Benfey et al. do not teach the complete claimed protein sequence. In fact, Benfey's sequence is just as flawed as Pysh's sequence, lacking the first 157 amino acid residues, and part of the first SCR domain. The present rejection attempts to make a case for obviousness merely by the finding of a partial sequence and armed with the knowledge that this partial sequence may be transformed into a plant and is then expressed in the roots, it would have been obvious to then isolate the complete coding sequence, and then transform and plant, and presumably, then test the plant for a useful function.

KSR: "[A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions". *Id.*, emphasis added. Benfey lacks a complete G922 sequence, and the partial sequence in Benfey lacks the instantly claimed function.

And, again, KSR established that: "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the art". *Id.*, at 1741. In this case, the partial protein taught by Benfey did not even measure up to the requirement of a complete element known in the art, the partial protein did not provide the instantly claimed function, the Examiner has provided no evidence or reasoning that the partial protein would provide the claimed function, and since no plant overexpressing the G922 sequence was known in the art, the cited elements should not be associated with each one another as the basis of an obviousness rejection according to the rationale set forth in KSR.


Finally, the Office action states that "it is not necessary that the prior art suggest the combination to achieve the same advantage." Perhaps, but the prior art should at least teach the respective elements of the combination. Having 67% of the instantly claimed protein, and having an incomplete SCR domain, Benfey does not.

Accordingly, Applicant respectfully requests that the rejection of the claims under 35 USC 103(a) be withdrawn.

CONCLUSION

Applicants believe that no additional fee is due with this communication. However, if the USPTO determines that an additional fee is due, the Commissioner is hereby authorized to charge Mendel Biotechnology, Inc. Deposit Account No. **50-1025**.

Respectfully submitted,
MENDEL BIOTECHNOLOGY, INC.



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